

Supplementary Information

Stable Production of Immortalized hPC-MSC-Derived Extracellular Vesicles: Integrated Cargo Analysis and Functional Validation

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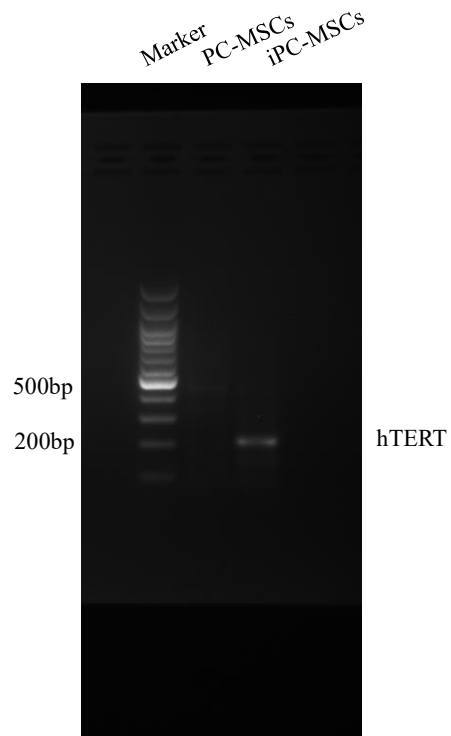
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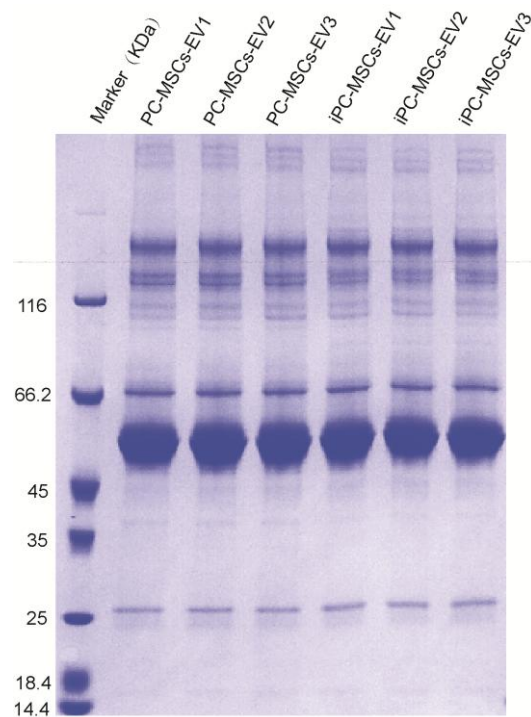
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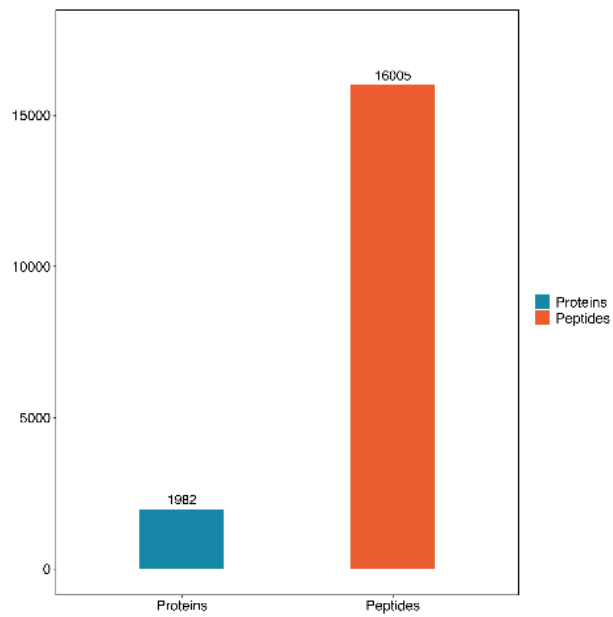
Supplementary Figures



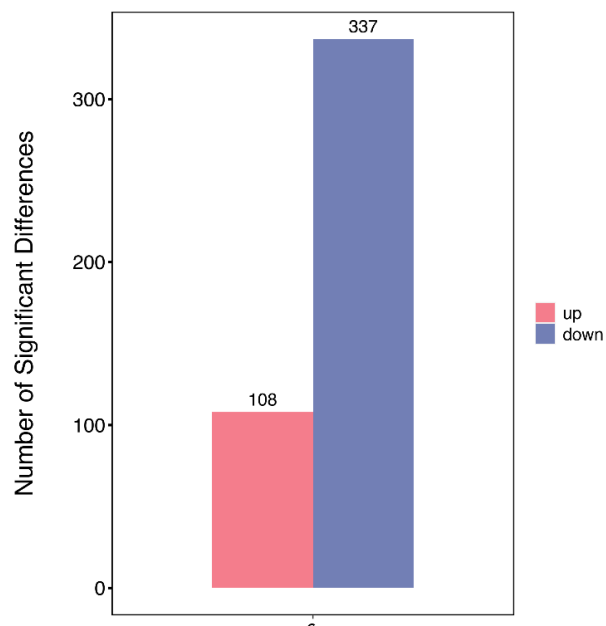
Supplementary Figure 1. RT-PCR validation of hTERT expression in cells was performed. The hTERT amplicon length is 209 bp. PC-MSCs at passage 3 and iPC-MSCs at passage 60.



Supplementary Figure 2. SDS-PAGE analysis results of extracellular vesicles derived from two cell lines. The molecular weights from top to bottom are: 116, 66.2, 45, 35, 25, 18.4, 14.4 (KDa).



Supplementary Figure 3. Statistical Chart of Basic Identification Results



Supplementary Figure 4. Histogram of differentially expressed proteins for the overall distribution of differentially expressed proteins. Differential proteins were screened for Foldchange ≥ 2 or Foldchange $\leq 1/2$ and p-value < 0.05 . Comparison group iPC-MSC-EV vs. PC-MSC-EV

Supplementary Table

Supplementary Table 1. The top 20 significantly upregulated and downregulated proteins

Gene Name	Description	log2FoldChange	Regulation	p-value
FSTL1	Follistatin-related protein 1	2.03	Up	1.31E-06
CCDC80	Coiled-coil domain-containing protein 80	5.97	Up	4.59E-06
ZYG11A	Protein zyg-11 homolog A	6.53	Up	5.04E-06
QSOX1	Sulfhydryl oxidase 1	1.28	Up	5.43E-06
EXT2	Exostosin-2	1.55	Up	6.85E-06
SMPD4	Sphingomyelin phosphodiesterase 4	5.30	Up	1.04E-05
AEBP1	Adipocyte enhancer-binding protein 1	4.78	Up	1.69E-05
CD55	Complement decay-accelerating factor	5.69	Up	2.40E-05
RPIA	Ribose-5-phosphate isomerase	4.76	Up	2.52E-05
GAK	Cyclin-G-associated kinase	4.47	Up	3.55E-05
BGN	Biglycan	2.42	Up	3.63E-05
CCN1	CCN family member 1	1.68	Up	5.68E-05
LOXL2	Lysyl oxidase homolog 2	1.58	Up	5.76E-05
MFAP5	Microfibrillar-associated protein 5	3.86	Up	6.62E-05
TRANK1	TPR and ankyrin repeat-containing protein 1	1.20	Up	8.08E-05
THBS1	Thrombospondin-1	1.09	Up	8.10E-05
CDH6	Cadherin-6	3.56	Up	8.44E-05
GAS6	Growth arrest-specific protein 6	4.15	Up	9.01E-05
HSPG2	Basement membrane-specific heparan sulfate proteoglycan core protein	1.50	Up	1.45E-04
CD59	CD59 glycoprotein	1.84	Up	1.73E-04
NIN	Ninein	-12.04	Down	1.79E-09
RTN4	Reticulon-4	-6.28	Down	2.03E-08
AFP	Alpha-fetoprotein	-7.53	Down	3.64E-08
EIF4A3	Eukaryotic initiation factor 4A-III	-4.96	Down	5.20E-08
EFNB1	Ephrin-B1	-5.00	Down	6.55E-08
SRCAP	Helicase SRCAP	-6.27	Down	7.27E-08
RNASE4	Ribonuclease 4	-6.60	Down	7.64E-08
UBA3	NEDD8-activating enzyme E1 catalytic subunit	-4.29	Down	9.24E-08
RHEB	GTP-binding protein Rheb	-4.79	Down	9.96E-08

ANP32B	Acidic leucine-rich nuclear phosphoprotein 32 family member B	-4.45	Down	1.07E-07
MMP3	Stromelysin-1	-4.80	Down	1.39E-07
STOML2	Stomatin-like protein 2, mitochondrial	-3.87	Down	1.41E-07
PSMD13	26S proteasome non-ATPase regulatory subunit 13	-3.90	Down	1.44E-07
PPIC	Peptidyl-prolyl cis-trans isomerase C	-3.99	Down	1.60E-07
PRKAG2	5'-AMP-activated protein kinase subunit gamma-2	-6.89	Down	1.65E-07
EXT1	Exostosin-1	-4.80	Down	1.94E-07
PDIA5	Protein disulfide-isomerase A5	-5.52	Down	2.59E-07
GRHPR	Glyoxylate reductase/hydroxypyruvate reductase	-4.17	Down	2.89E-07
PDCD5	Programmed cell death protein 5	-4.38	Down	3.34E-07
FGB	Fibrinogen beta chain	-6.11	Down	3.39E-07

Supplementary Table 2. Szapiel scoring system

Degree of alveolitis	Histopathological features
0	Normal lung tissue
1	Mild alveolitis (+), widened inflammatory cell infiltrate at alveolar septa, <20% of area involved Lung lobes
2	Moderate alveolitis (++), 20% to 50% of lung lobes involved
3	Severe alveolitis (++++), with involvement of >50% of lung lobes

Supplementary Table 3. Ashcroft scores

PF Degree	Histopathological features
0	Normal lung tissue
1	Mild fibrosis of fine bronchial and alveolar walls
3	Moderate fibrosis of fine bronchioles and alveolar walls without significant structural destruction of lung tissue
5	Marked fibrosis with structural destruction of lung tissue and formation of fibrous bands or fibrous nodules
7	Severe structural deformation of lung tissue or the presence of large fibrous foci
8	Fibrotic lesions are present throughout the visual field